

IT IS CLAIMED:

1. An article for use in an aerosol device, for producing an aerosol, comprising
  - (a) a heat-conductive substrate having an exterior surface with a selected surface area, and
  - (b) a drug composition film on the exterior surface, the film having a selected film thickness of between 0.05 and 20  $\mu\text{m}$ , where
    - (i) the film thickness is such that an aerosol formed by vaporizing the drug composition by heating the substrate and condensing the vaporized drug composition contains 10% by weight or less drug-degradation products and at least 50% of the total amount of drug composition in the film, and
    - (ii) the selected substrate surface area is such as to yield an effective human therapeutic dose of the drug aerosol.
2. The article of claim 1, wherein said selected substrate surface area is between about 0.05-100  $\text{cm}^2$ .
3. The article of claim 1, wherein said substrate exterior surface is impermeable.
4. The article of claim 1, wherein said substrate is a material selected from the group consisting of metals, polymers, ceramics, and glass.
5. The article of claim 4, wherein said substrate is metal and said metal is stainless steel or aluminum.
6. The article of claim 1, wherein said substrate has a contiguous surface area of greater than 1  $\text{mm}^2$  and a material density of greater than 0.5 g/cc.
7. The article of claim 1, wherein the film thickness has been selected such that the drug composition film can be volatilized from the substrate with less than 5% by weight drug degradation products.

8. The article of claim 1, wherein the drug is one that when vaporized from a drug composition film on an impermeable surface of a heat conductive substrate and condensed to form aerosol particles, under selected vaporization conditions that lead to at least 50% recovery of drug in the aerosol, the aerosol produced exhibits (i) less than about 5% by weight drug degradation products when the drug composition is vaporized from a film having a selected film thickness between 0.05 and 20 microns, and (ii) increasing levels of drug degradation products, with increasing film thickness above the selected film thickness.

9. The article of claim 1, wherein said compound is selected from the group consisting of the following, where for each compound, there is shown a range of film thickness within which the corresponding compound film thickness is selected:

- (1) alprazolam, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (2) amoxapine, film thickness between 2 and 20  $\mu\text{m}$ ;
- (3) atropine, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (4) bumetanide film thickness between 0.1 and 5  $\mu\text{m}$ ;
- (5) buprenorphine, film thickness between 0.05 and 10  $\mu\text{m}$ ;
- (6) butorphanol, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (7) clomipramine, film thickness between 1 and 8  $\mu\text{m}$ ;
- (8) donepezil, film thickness between 1 and 10  $\mu\text{m}$ ;
- (9) hydromorphone, film thickness between 0.05 and 10  $\mu\text{m}$ ;
- (10) loxapine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (11) midazolam, film thickness between 0.05 and 20  $\mu\text{m}$ ;
- (12) morphine, film thickness between 0.2 and 10  $\mu\text{m}$ ;
- (13) nalbuphine, film thickness between 0.2 and 5  $\mu\text{m}$ ;
- (14) naratriptan, film thickness between 0.2 and 5  $\mu\text{m}$ ;
- (15) olanzapine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (16) paroxetine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (17) prochlorperazine, film thickness between 0.1 and 20  $\mu\text{m}$ ;
- (18) quetiapine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (19) sertraline, film thickness between 1 and 20  $\mu\text{m}$ ;
- (20) sibutramine, film thickness between 0.5 and 2  $\mu\text{m}$ ;
- (21) sildenafil, film thickness between 0.2 and 3  $\mu\text{m}$ ;
- (22) sumatriptan, film thickness between 0.2 and 6  $\mu\text{m}$ ;

- (23) tadalafil, film thickness between 0.2 and 5  $\mu\text{m}$ ;
- (24) vardenafil, film thickness between 0.1 and 2  $\mu\text{m}$ ;
- (25) venlafaxine, film thickness between 2 and 20  $\mu\text{m}$ ;
- (26) zolpidem, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (27) apomorphine HCl, film thickness between 0.1 and 5  $\mu\text{m}$ ;
- (28) celecoxib, film thickness between 2 and 20  $\mu\text{m}$ ;
- (29) ciclesonide, film thickness between 0.05 and 5  $\mu\text{m}$ ;
- (30) eletriptan, film thickness between 0.2 and 20  $\mu\text{m}$ ;
- (31) parecoxib, film thickness between 0.5 and 2  $\mu\text{m}$ ;
- (32) valdecoxib, film thickness between 0.5 and 10  $\mu\text{m}$ ; and
- (33) fentanyl, film thickness between 0.05 and 5  $\mu\text{m}$ .

10. A method of forming the article of claim 1, comprising

- (a) for a selected drug composition, determining a film thickness between 0.05 and 20 microns such that an aerosol formed by (i) vaporizing the drug composition by heating a heat-conductive substrate having an exterior surface and a film of the drug composition on the substrate surface, and (ii) condensing the vaporized drug composition contains 10% by weight or less drug degradation products and at least 50% of the total amount of drug composition in the film,
- (b) determining a substrate surface area that, when a film of the drug composition of the determined thickness is applied to said area, accommodates an effective human therapeutic inhalation dose of drug in the drug composition, and
- (c) forming a film of the selected drug composition of the identified thickness over the determined substrate area.

11. The method of claim 10, wherein the determined film thickness is such that the aerosol formed by so vaporizing and condensing the drug composition contains less than 5% by weight drug-degradation product.

12. The method of claim 10, wherein the drug composition is one that, when vaporized from a drug composition film formed on an impermeable surface of a heat conductive substrate and condensed to form aerosol particles, under selected vaporization conditions that lead to at least 50% recovery of the drug composition in the aerosol particles, exhibits (i) less than 5% by weight drug degradation products in

aerosol particles when the compound is vaporized from a film having a selected film thickness between 0.05 and 20 microns, and (ii) increasing levels of drug degradation products in the aerosol particles, with increasing film thickness above the selected film thickness.

13. The method of claim 10, wherein said drug composition, and the range of film thicknesses within which a film thickness is to be determined, is selected from the group consisting of:

- (1) alprazolam, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (2) amoxapine, film thickness between 2 and 20  $\mu\text{m}$ ;
- (3) atropine, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (4) bumetanide film thickness between 0.1 and 5  $\mu\text{m}$ ;
- (5) buprenorphine, film thickness between 0.05 and 10  $\mu\text{m}$ ;
- (6) butorphanol, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (7) clomipramine, film thickness between 1 and 8  $\mu\text{m}$ ;
- (8) donepezil, film thickness between 1 and 10  $\mu\text{m}$ ;
- (9) hydromorphone, film thickness between 0.05 and 10  $\mu\text{m}$ ;
- (10) loxapine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (11) midazolam, film thickness between 0.05 and 20  $\mu\text{m}$ ;
- (12) morphine, film thickness between 0.2 and 10  $\mu\text{m}$ ;
- (13) nalbuphine, film thickness between 0.2 and 5  $\mu\text{m}$ ;
- (14) naratriptan, film thickness between 0.2 and 5  $\mu\text{m}$ ;
- (15) olanzapine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (16) paroxetine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (17) prochlorperazine, film thickness between 0.1 and 20  $\mu\text{m}$ ;
- (18) quetiapine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (19) sertraline, film thickness between 1 and 20  $\mu\text{m}$ ;
- (20) sibutramine, film thickness between 0.5 and 2  $\mu\text{m}$ ;
- (21) sildenafil, film thickness between 0.2 and 3  $\mu\text{m}$ ;
- (22) sumatriptan, film thickness between 0.2 and 6  $\mu\text{m}$ ;
- (23) tadalafil, film thickness between 0.2 and 5  $\mu\text{m}$ ;
- (24) vardenafil, film thickness between 0.1 and 2  $\mu\text{m}$ ;
- (25) venlafaxine, film thickness between 2 and 20  $\mu\text{m}$ ;
- (26) zolpidem, film thickness between 0.1 and 10  $\mu\text{m}$ ;

- (27) apomorphine HCl, film thickness between 0.1 and 5  $\mu\text{m}$ ;
- (28) celecoxib, film thickness between 2 and 20  $\mu\text{m}$ ;
- (29) ciclesonide, film thickness between 0.05 and 5  $\mu\text{m}$ ;
- (30) eletriptan, film thickness between 0.2 and 20  $\mu\text{m}$ ;
- (31) parecoxib, film thickness between 0.5 and 2  $\mu\text{m}$ ;
- (32) valdecoxib, film thickness between 0.5 and 10  $\mu\text{m}$ ; and
- (33) fentanyl, film thickness between 0.05 and 5  $\mu\text{m}$ .

14. The method of claim 10 wherein said substrate surface area is between about 0.05-100  $\text{cm}^2$ .

15. A method of forming an effective human therapeutic inhalation dose of a drug composition aerosol having 10% or less drug degradation products and an aerosol particle mass median aerodynamic diameter (MMAD) between 0.01 and 3  $\mu\text{m}$ , comprising

heating the substrate in the article of claim 1 to a temperature between 300°C and 500°C, thereby vaporizing a drug composition film on the substrate, and

flowing a gas during said heating across the substrate at a gas flow rate effective to produce a desired size of aerosol particles by condensation.

16. The method according to claim 15, wherein said heating vaporizes the drug composition film on the substrate within a time period of 2 seconds.

17. The method according to claim 16, wherein said heating vaporizes the drug composition film on the substrate within a time period of 0.5 seconds.

18. The method of claim 15, wherein said flowing is at a gas flow rate of between 4 and 50 L/minute.

19. The method of claim 15, wherein the drug composition film has a thickness on the substrate such that the aerosol contains 5% or less drug degradation products.

20. The method of claim 19, wherein the drug composition is one that when vaporized from a drug composition film on an impermeable surface of a heat conductive substrate and condensed to form aerosol particles, under selected vaporization conditions that lead to at least 50% recovery of drug composition in the aerosol particles, the aerosol produced exhibits (i) less than about 5% by weight drug degradation products when the drug composition is vaporized from a film having a selected film thickness between 0.05 and 20 microns, and (ii) increasing levels of drug degradation products, with increasing film thickness above the selected film thickness.

21. The method of claim 15, wherein said drug composition is selected from the group consisting of the following, where for each drug composition, there is shown a range of film thickness within which the corresponding drug composition film thickness is selected:

- (1) alprazolam, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (2) amoxapine, film thickness between 2 and 20  $\mu\text{m}$ ;
- (3) atropine, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (4) bumetanide film thickness between 0.1 and 5  $\mu\text{m}$ ;
- (5) buprenorphine, film thickness between 0.05 and 10  $\mu\text{m}$ ;
- (6) butorphanol, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (7) clomipramine, film thickness between 1 and 8  $\mu\text{m}$ ;
- (8) donepezil, film thickness between 1 and 10  $\mu\text{m}$ ;
- (9) hydromorphone, film thickness between 0.05 and 10  $\mu\text{m}$ ;
- (10) loxapine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (11) midazolam, film thickness between 0.05 and 20  $\mu\text{m}$ ;
- (12) morphine, film thickness between 0.2 and 10  $\mu\text{m}$ ;
- (13) nalbuphine, film thickness between 0.2 and 5  $\mu\text{m}$ ;
- (14) naratriptan, film thickness between 0.2 and 5  $\mu\text{m}$ ;
- (15) olanzapine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (16) paroxetine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (17) prochlorperazine, film thickness between 0.1 and 20  $\mu\text{m}$ ;
- (18) quetiapine, film thickness between 1 and 20  $\mu\text{m}$ ;
- (19) sertraline, film thickness between 1 and 20  $\mu\text{m}$ ;
- (20) sibutramine, film thickness between 0.5 and 2  $\mu\text{m}$ ;

- (21) sildenafil, film thickness between 0.2 and 3  $\mu\text{m}$ ;
- (22) sumatriptan, film thickness between 0.2 and 6  $\mu\text{m}$ ;
- (23) tadalafil, film thickness between 0.2 and 5  $\mu\text{m}$ ;
- (24) vardenafil, film thickness between 0.1 and 2  $\mu\text{m}$ ;
- (25) venlafaxine, film thickness between 2 and 20  $\mu\text{m}$ ;
- (26) zolpidem, film thickness between 0.1 and 10  $\mu\text{m}$ ;
- (27) apomorphine HCl, film thickness between 0.1 and 5  $\mu\text{m}$ ;
- (28) celecoxib, film thickness between 2 and 20  $\mu\text{m}$ ;
- (29) ciclesonide, film thickness between 0.05 and 5  $\mu\text{m}$ ;
- (30) eletriptan, film thickness between 0.2 and 20  $\mu\text{m}$ ;
- (31) parecoxib, film thickness between 0.5 and 2  $\mu\text{m}$ ;
- (32) valdecoxib, film thickness between 0.5 and 10  $\mu\text{m}$ ; and
- (33) fentanyl, film thickness between 0.05 and 5  $\mu\text{m}$ .

22. A method of forming an article for use in an aerosol device, for producing aerosol particles, comprising

(a) preparing on a heat-conductive substrate a drug composition film having a first film thickness;

(b) heating said substrate to vaporize said drug composition film and cooling, thereby producing aerosol particles containing said drug composition;

(c) determining (i) the purity of said aerosol particles and (ii) the fraction of film vaporized, and

(d) repeating steps (a) – (c) one or more times but at a film thickness different from said first film thickness to achieve an aerosol particle purity of at least 90% and a fraction of drug composition film vaporized of at least 50%.

23. The method of claim 22, wherein said substrate has an impermeable surface on which the drug composition film is prepared.

24. The method of claim 22, wherein said substrate has contiguous surface area of greater than 1  $\text{mm}^2$  and a material density of greater than 0.5 g/cc.

25. The method of claim 22, wherein said determining further comprises selecting a drug composition yielding an aerosol particle purity of equal to or

greater than 60% by weight but less than 90% by weight and a fraction of film vaporized of greater than 30% for said step of repeating.

26. The method of claim 22, wherein said preparing includes preparing a drug composition film on a selected surface area of said substrate sufficient to provide a therapeutic dose of drug in the drug composition as aerosol particles.

27. The method of claim 22, wherein said heating is in an inert atmosphere.

28. The method of claim 22, wherein said preparing comprises preparing a drug composition film having a first film thickness of between 1-20  $\mu\text{m}$ .

29. The method of claim 28, wherein said repeating comprises preparing a drug composition film having a different film thickness of between 0.05-10  $\mu\text{m}$ .

30. The method of claim 22, wherein said compound is selected from the group consisting of adenosine, amoxapine, apomorphine, aripiprazole, aspirin, astemizole, atenolol, benazepril, benztropine, bromazepam, budesonide, buspirone, caffeine, captopril, carbamazepine, cinnarizine, clemastine, clemastine fumarate, clofazimine, desipramine, dipyridamole, dolasetron, doxylamine, droperidol, enalapril maleate, fluphenazine, flurazepam, flurbiprofen, fluvoxamine, frovatriptan, hydroxyzine, ibutilide, indomethacine norcholine ester, ketorolac, ketorolac norcholine ester, levodopa, melatonin, methotrexate, methysergide, metoclopramide, nabumetone, naltrexone, nalmefene, perphenazine, pimozide, piroxicam, pregnanolone, prochlorperazine 2HCl, protriptyline HCl, protriptyline, pyrilamine, pyrilamine maleate, quinine, ramipril, risperidone, scopolamine, sotalol, sulindac, terfenadine, triamcinolone acetonide, trihexyphenidyl, thiothixene, telmisartan, temazepam, triamterene, trimipramine, ziprasidone, and zonisamide.